ELSEVIER

Journal of Hepatology 49 (2008) 658–663

Journal of Hepatology

www.elsevier.com/locate/jhep

Letters to the Editor

Doppler ultrasonography for the diagnosis of liver vascular malformations in hereditary hemorrhagic telangiectasia

To the Editor:

We read with interest the paper by Buonamico et al. [1] regarding Doppler ultrasonography (US) for the diagnosis of liver vascular malformations (VMs) in hereditary hemorrhagic telangiectasia (HHT). Doppler US has been proposed for the detection of liver VMs in HHT for the last 15 years [2,3]; the test's parameters have shown excellent sensitivity and specificity [3,4], and thus it has been confirmed as a first-line imaging technique for liver VMs in HHT [5].

The present study offers further validation of the diagnostic accuracy of Doppler US for liver VMs in HHT against a reference technique (multi-slice CT, MSCT). Liver MSCT has been used for an extensive study of HHT families [6], but the accuracy of this technique remains to be demonstrated, as it was a descriptive study without a standard of reference. The use of CT as the reference standard for the diagnosis of liver VMs is thus debatable, as one wonders whether every incongruous result is due to an error of either the technique under trial or the "reference" technique. This question applies to the nine cases in which the so-called "color spot sign" proved positive but the classification was false-positive (as CT was negative) [1]. We wonder if these cases were actually in fact, misdiagnoses by CT, particularly since the Authors used a 4-detector CT scanner, which is not the best available technology, especially for detection of tiny vascular anomalies.

The Authors describe color spots as a sign of liver VMs in HHT, but it seems rather a new name for an already-reported sign. We have described with a Doppler study tortuous small arterial branches with a low resistivity index (RI) [7], with imaging findings strictly superimposable to those listed by Authors in their Figs. 4A, B and C; this aspect is even better shown with the newer energy Doppler technologies [8]. This sign has previously been referred to by the term *peripheral hypervascularization* [7], which seems more appropriate than the term "color spot", as these micro-VMs are typically depicted as tiny, "spider-like" vessels [7,8]. Peripheral hypervascularization is one of the elements contributing to the severity grading of hepatic VMs in HHT [7,8]. In the earliest stage of liver VMs (grade 0 + by our classification [7]), peripheral vascularization has to be carefully sought out; otherwise, sufficient Doppler US data might be lacking. On the other hand, the term *hepatic hypervascularization*, which has been used by Caselitz et al. [4] and not by us, includes the whole spectrum of intrahepatic abnormalities of hepatic artery branches (from grades 2 to 4 of our classification). Whereas *peripheral hypervascularization* refers to small peripheral VMs, *hepatic hypervascularization* refers to obvious, prominent vascular abnormalities: it thus seems misleading to use this term for small VMs, as proposed by Buonamico et al.

The Authors claim a low sensitivity for extrahepatic parameters, the main one being the diameter of the hepatic artery. Actually, they have used for this study a cut-off value (>7 mm) that was calculated as a threshold with 100% specificity and sensitivity on the basis of findings in 25 subjects with severe vascular abnormalities [4]. It is clear that using US criteria derived from such a population entails the risk of a low diagnostic sensitivity when applied to the screening of a general HHT population. On the other hand, the proposed cut-off value of >6 mm [3,7] for the hepatic artery diameter has no overlap with normal subjects in the series by Buonamico and Caselitz [1,4]. This cut-off value would have allowed for the diagnosis of the majority of the MSCT-positive patients of the Buonamico et al. series; almost all of the cases would have been identified by using the criteria of our classification [7], including those at stage 0 + (HA diameter >5 < 6 mm).

Evaluation of the proper hepatic artery can give important information about hepatic circulation, and we agree with the Authors' hypothesis, already reported in 1997 [3], that morphologic and flow changes found in the extrahepatic artery depend on increased hepatic blood flow through VMs, even when they are microscopic. Doppler US diagnosis of liver VMs in HHT requires a combination of extrahepatic and intrahepatic findings [7], which can provide a diagnostic accuracy ranging between 95% and 99% for different observers [8].

References

[1] Buonamico P, Suppressa P, Lenato GM, Pasculli P, D'Ovidio F, Memeo M, et al. Liver involvement in a large cohort of patients with hereditary hemorrhagic telangiectasia: echo-color-Doppler vs multislice computed tomography study. J Hepatol 2008;48:811–820.

[2] Buscarini E, Buscarini L, Civardi G, Arruzzoli S, Bossalini G, Piantanida M. Hepatic vascular malformations in hereditary hemorrhagic telangiectasia: imaging findings. AJR 1994;163:1105–1110.

[3] Buscarini E, Buscarini L, Danesino C, Piantanida M, Civardi G, Quaretti P, et al. Hepatic vascular malformations in hereditary hemorrhagic telangiectasia: Doppler sonographic screening in a large family. J Hepatol 1997;26:111–118.

[4] Caselitz M, Bahr MJ, Bleck JS, Chavan A, Manns MP, Wagner S, et al. Sonographic criteria for the diagnosis of hepatic involvement in hereditary hemorrhagic telangiectasia (HHT). Hepatology 2003;37:1139–1146.

[5] Buscarini E, Plauchu H, Garcia Tsao G, White Jr RI, Sabba' C, Miller F, et al. Liver involvement in hereditary hemorrhagic telangiectasia: consensus recommendations. Liver Int 2006;26:1040–1046.

[6] Ianora AA, Memeo M, Sabba' C, Cirulli A, Rotondo A, Angelelli G. Hereditary hemorrhagic telangiectasia: multi-detector row helical CT assessment of hepatic involvement. Radiology 2004;230:250–259.

[7] Buscarini E, Danesino C, Olivieri C, Lupinacci G, De Grazia F, Reduzzi L, et al. Doppler ultrasonographic grading of hepatic vascular malformations in hereditary hemorrhagic telangiectasia – results of extensive screening. Ultraschall Med 2004;25:348–355.

[8] Buscarini E, Gebel M, Ocran K, Manfredi G, Del Vecchio Blanco G, Stefanov R, et al. Interobserver agreement in diagnosing liver involvement in hereditary hemorrhagic telangectasia by Doppler ultrasound. Ultrasound Med Biol 2008;34:718–725.

Elisabetta Buscarini
Guido Manfredi
Alessandro Zambelli
Gastroenterology Department,
Center for the Diagnosis,
Therapy and Surveillance of HHT,
Maggiore Hospital,
Largo Dossena 2,
26013 Crema, Italy
E-mail address: ebuscarini@rim.it

doi:10.1016/j.jhep.2008.06.007

New signs and old applications of echo-color-Doppler should always be compared to a gold standard

To the Editor:

We thank our colleagues for the comments to our paper, which allow us to better clarify some aspects regarding the US diagnosis of liver involvement in hereditary hemorrhagic teleangiectasia (HHT) patients.

In our study, we described a new Doppler sign, called 'color-spot', particularly suitable for identifying small hepatic arterio-venous malformations (HAVMs) and verified its accuracy using multislice CT (MSCT) as gold standard [1]. Moreover, we clearly distinguished the *color-spots* found in the peripheral subcapsular region of the liver from '*hepatic hypervascularization*', a sign previously reported by Caselitz et al. [2]. Both are suggestive of small HAVMs and provide a greater diagnostic sensitivity for HAVMs in HHT when compared to previously published extrahepatic parameters.

It must be emphasized that the diagnostic sensitivity and accuracy of previous ultrasound (US) findings [2–4] cannot be defined since their results were not systematically compared to a gold standard; in fact, Doppler-negative HHT patients have never been systematically compared with other techniques. Ours is the first controlled study to assess the diagnostic accuracy of Doppler US for diagnosis of HAVMs in HHT with respect to MSCT as a reference technique. According to Buscarini et al., the use of CT as gold standard is debatable, as we employed a 4-detector CT scanner which is not the best available technology; however, these authors did not consider that our prospective study was conducted over a four-year period. Having initiated our study with a 4-detector CT scan and in order to avoid inter-equipment variability [5], we preferred to prospectively study a large patient sample maintaining the same methodology, even if meanwhile a more sophisticated 16-detector scan had become available (moreover, our HHT-experienced radiologists have not found any difficulties in identifying tiny vascular abnormalities with both CT scanner systems).

The two signs (*color-spot* described by our group and *peripheral hypervascularization* reported by Buscarini et al. [4]) are two distinct echo-color-Doppler parameters. The *color-spot* sign appears in the presence of isolated spotty-like images with a high blood-flow velocity and a resistive index (RI) less than 0.45. It corresponds to a point on a very small peripheral tortuous arterial vessel where, due to a Doppler angle close to zero, the high Doppler frequency shift overcomes the threshold of detection, thus giving rise to a visible spotty-like image (whereas the remaining tract of the vessel, characterized by an unfavourable Doppler angle, undergoes a reduction in the intensity of the ultrasound